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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BLANCHARD, DAVID J	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 11/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/981,915	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	David J. Blanchard	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 September 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *58-65 and 68-75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *63-65 and 68* is/are allowed.

6)☒ Claim(s) *58-62 and 69-75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/13/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-57 and 66-67 are cancelled.

Claims 58-65 and 69 has been amended.

Claims 71-75 have been added.

2. Claims 58-65 and 68-75 are pending and under examination.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. This office Action contains New Grounds of Rejections.

Information Disclosure Statement

5. The information disclosure statement (IDS) submitted on 9/13/05 has been considered by the Examiner. A signed copy of the IDS accompanies this Office Action.

Rejections/Objections Withdrawn

6. The objections to the specification for various formal matters requiring correction are withdrawn in view of the amendments to the specification.

7. The rejection of claims 58-63, 66-67 and 69-70 under 35 U.S.C 112, second paragraph, as the being indefinite in the recitation of an "extracellular domain" optionally lacking its associated signal peptide is withdrawn in view of the amendments to the claims.

8. The rejection of claim 70 under 35 U.S.C 112, second paragraph, as the being indefinite in the recitation of an "epitope tag" is withdrawn in view of the amendments to the claims.

9. The rejection o claims 58-63 and 68-70 under 35 U.S.C. 112, first paragraph is withdrawn in view of applicant's successful completion of the deposit requirements.

10. The rejection of claims 58-62 and 69-70 under 35 U.S.C 112, first paragraph, for lack of enablement is withdrawn in view of Applicant's arguments.

Response to Arguments

11. The rejection of claims 58-62, 69-70 and applied to newly added claims 71-75 under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement is maintained.

The response filed 9/13/05 states that as presently amended the claims are drawn to polypeptides having at least 80% amino acids sequence identity to the polypeptide of SEQ ID NO:523 wherein the polypeptide induces chondrocyte re-differentiation or wherein the polypeptide induces proliferation of rat utricular supporting cells. Applicant argues that Example 126 of the present specification (page 351) and Example 116 of the present application (page 347) provide the protocols and sufficient guidance for the chondrocyte re-differentiation assay and the proliferation of rat utricular supporting cells assay and following this guidance one skilled in the art can easily test whether a variant of PRO337 induces chondrocyte re-differentiation or induces proliferation of rat utricular supporting cells. The response also states that the

specification describes methods for determining the percent identity between two sequences and provides detailed guidance as to changes that may be made to a PRO polypeptide without adversely affecting its activity (see pages 180-183). In response, Applicant's arguments appear to go more towards enablement and not the disputed issue of written description. Applicant is reminded that the written description requirement is separate and distinct from the enablement requirement. In re Barker, 559 F.2d 588, 194 USPQ 470 (CCPA 1977), cert. denied, 434 U.S. 1064 (1978); Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1562, 19 USPQ2d 1111, 1115 (Fed. Cir. 1991)). See MPEP 2161.

The specification discloses that the PRO337 polypeptide (SEQ ID NO:523) is a newly identified member of the IgLON sub family of the immunoglobulin superfamily and may posses neurite growth and differentiation potentiating properties (see page 179). The specification discloses that the PRO337 polypeptide was positive for the proliferation of rat utricular supporting cells (assay 54 at page 347) and thus, acts as a mitogen for inner ear supporting cells and PRO337 was positive in the chondrocyte re-differentiation assay.

The specification does not provide sufficient written description as to the structural features of the claimed genus of PRO337 polypeptides and the correlation between the chemical structure and function of the genus of PRO337 polypeptides, such as structural domains or motifs that are conserved or essential for activity and could distinguish members of the genus from those excluded. The specification does

not disclose a single species with less than 100% sequence identity with PRO337 and having the recited biological activity.

An adequate written description of a chemical invention requires a precise definition, such as by structure, formula, chemical name, or physical properties, and not merely a wish or plan for obtaining the chemical invention claimed. See, e.g., Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004) (The patent at issue claimed a method of selectively inhibiting PGHS-2 activity by administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product, however the patent did not disclose any compounds that can be used in the claimed methods. While there was a description of assays for screening compounds to identify those that inhibit the expression or activity of the PGHS-2 gene product, there was no disclosure of which peptides, polynucleotides, and small organic molecules selectively inhibit PGHS-2. The court held that "[w]ithout such disclosure, the claimed methods cannot be said to have been described."). Similarly, in the present case the disclosure of protocols and guidance for testing PRO337 polypeptides for the recited activity, where there is no disclosure of which PRO337 polypeptide variants induce chondrocyte re-differentiation or induce proliferation of rat utricular supporting cells is merely a wish or plan for obtaining the PRO337 polypeptides claimed and is insufficient to describe the genus of PRO337 polypeptides.

Conception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. When an inventor is

unable to envision the detailed constitution of a polypeptide so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e., until after the polypeptide has been isolated. In such instances the alleged conception fails not merely because the field is unpredictable or because of the general uncertainty surrounding experimental sciences, but because the conception is incomplete due to factual uncertainty that undermines the specificity of the inventor' s idea of the invention. *Burroughs Wellcome Co. v. Barr Laboratories Inc.*, 40 F.3d 1223, 1229, 32 USPQ2d 1915, 1920 (Fed. Cir. 1994). Reduction to practice in effect provides the only evidence to corroborate conception (and therefore possession) of the invention.

Accordingly, the rejection of claims 58-62 and 69-75 for lack of adequate written description is maintained.

12. The rejection of claims 58-61 and applied to newly added claims 71-74 under 35 U.S.C 102(b) as being anticipated by Struyk et al (The Journal of Neuroscience 15(3):2141-2156, 1995) is maintained.

The response filed 9/13/05 reiterates that a claim is not anticipated unless each and every element of the claim is found, either expressly or inherently in a single prior art reference. The response argues that the polypeptide of Struyk et al does not have the presently recited functions, i.e., inducing chondrocyte re-differentiation or inducing proliferation of rat utricular supporting cells. Applicant discusses the expression of the polypeptide of Struyk et al and asserts that since the polypeptide is not expressed in

other types of cells such as chondrocytes or rat utricular supporting cells, it is highly improbable that it induces chondrocyte re-differentiation or induces proliferation of rat utricular cells. First, it is important to note that the recited PRO337 polypeptides are also not expressed in chondrocytes or rat utricular supporting cells, but were added to cultures of chondrocytes or rat utricular supporting cells and assayed (see pages 347 and 351). Additionally, the polypeptide ("neurotrimin") taught by Struyk et al is substantially identical in structure, i.e., 97% amino acid identity with the mature polypeptide of SEQ ID NO:523 (lacking the signal sequence; residues 1-28 of SEQ ID NO:523), which is the active form of PRO337. Further, the specification discloses PRO337 as a newly identified member of the IgLON sub family of the immunoglobulin superfamily (Ig-SF) and suggests it may possess neurite growth and differentiation potentiating properties (see page 179) and Struyk et al teach that the neurotrimin polypeptide is a member of the Ig-SF, which is a family of proteins frequently implicated in neural cell interactions and nerve fiber outgrowth during development and the expression of neurotrimin appears to correlate with the development of several neural circuits (see bridging paragraph of pages 2141-2142 and top right column at page 2154). Thus, one of ordinary skill in the art would reasonably conclude that the neurotrimin polypeptide of Struyk et al is identical to PRO337 claimed, considering the substantial structural identity, both polypeptides belong to the Ig-SF and the common suggestion that both polypeptides possess neural growth and differentiation properties. Applicant is reminded that where the claimed and prior art products are identical or substantially identical in structure or composition, a prima facie case of either

anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. In re Best, 562 F.2d at 1255, 195USPQ at 433. (see MPEP 2112.01). Thus, absent objective evidence to the contrary, it is the Examiner's position that the neurotrimin polypeptide taught by Struyk et al possesses the same structural and functional properties as those of the PRO337 polypeptides claimed.

For these reasons the rejection is maintained.

13. The rejection of claims 58-61 and 69-70 and applied to newly added claims 71-74 under 35 U.S.C. 103(a) as being unpatentable over Struyk et al (The Journal of Neuroscience 15(3):2141-2156, 1995) in view of Grose (US Patent 5,710,248) is maintained.

The response filed 9/13/05 argues as above, stating that Struyk et al do not teach each and every limitation of the claims, i.e., Struyk does not teach a polypeptide that induces chondrocyte re-differentiation or induces proliferation of rat utricular supporting cells and Grose does not cure the deficiencies of Struyk. In response to this

argument the Examiner's arguments above for Struyk apply here as well and the rejection is maintained.

14. Claims 58-62 and 69-75 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are indefinite in the recitation of "An isolated polypeptide... comprising a polypeptide" because it is unclear whether the claims are drawn to a polypeptide comprising the recited amino acid sequences or if the claims are drawn to a fusion polypeptide comprising at least two polypeptides wherein one of the polypeptides comprises a polypeptide having the recited amino acid sequences. One of skill in the art would not be reasonably apprised of the metes and bounds of the structural limitations of the claimed polypeptides because there is ambiguity in what additional polypeptide or polypeptides may or may not be present. Amending the claims to recite "An isolated polypeptide having at least 80% amino acid sequence identity to:", for example, would obviate this rejection.

Conclusions

15. Claims 63-65 and 68 are free of the prior art and are in condition for allowance.

16. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832. The official fax number for the organization where this application or proceeding is assigned is 571-273-8300. Any inquiry of a general nature, matching or filed papers or relating to the status of this application or proceeding should be directed to Tony Parks for Art Unit 1643 whose telephone number is 571-272-0543.

Respectfully,
David J. Blanchard
571-272-0827

SHEELA HUFF
PRIMARY EXAMINER